

THE HUMAN KALLIKREIN GENE LOCUS - DISCOVERY OF SIX NEW GENES

George M. Yousef, Liu-Ying Luo and Eleftherios P. Diamandis. Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Ontario and Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada.

The human kallikrein gene family on chromosome 19q13.3-13.4 currently includes three genes, KLK1 (pancreatic/renal kallikrein), KLK2 (human glandular kallikrein) and KLK3 (PSA, prostate-specific antigen). More recently, two additional genes have been mapped to the same region, Zyme/protease M/neurosin and the normal epithelial cell-specific gene 1 (NES1). These serine proteases are regulated by steroid hormones and PSA, Zyme and NES1, are all known to be downregulated in breast cancer. In an effort to map known kallikrein-like genes and identify new kallikrein-like genes, we analyzed a linear genomic region of ~ 300 Kb around chromosome 19q13.3-q13.4. We were able to define the precise location of all known genes, map the location of another three known genes (stratum corneum chymotryptic enzyme, SCCE, neurosin and trypsin-like serine protease, TLSP) and discover six additional genes (KLK-L1, KLK-L2, KLK-L3, KLK-L4, KLK-L5 and UG) of which the first five are serine proteases with homology to other kallikreins. The UG gene is homologous to human myeloid surface antigen CD33 and to human leptin-binding proteins 1 and 2. All these genes are aligned as follows on 19q13.3-q13.4:

Centromere - PSA - KLK2 - KLK-L1 - KLK-L2 - Zyme- SCCE - Neurosin - KLK-L3 - NES1 - TLSP - KLK-L4 - KLK-L5 - UG - telomere. Given the implications of the known kallikreins in breast and prostate cancer, we speculate that some of the newly identified genes may have similar utility. UG may be implicated in leptin metabolism. We conclude that the kallikrein locus in humans consists of at least thirteen homologous genes.